

**Patel et al. - Quantifying and understanding the higher risk of atherosclerotic cardiovascular disease among South Asians — results from the UK Biobank prospective cohort study**

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## Supplemental Methods:

### *Study population:*

The UK Biobank is a prospective cohort study that enrolled over 500,000 individuals between the ages of 40 and 69 years between 2006 and 2010.<sup>32,33</sup> Within this cohort, a subset of 481,542 participants self-reported South Asian or European ancestry. South Asian ancestry was defined as self-identification as being of Indian, Pakistani, Bangladeshi origin or reporting other South Asian origin with country of birth as Bhutan, Maldives, Nepal, or Sri Lanka. European ancestry was based on self-identification as being white British, white Irish, or any other white European background.

After additional exclusion of 24,069 individuals with atherosclerotic cardiovascular disease (ASCVD) diagnosed prior to enrollment, 457,473 individuals were included in subsequent analyses. Exclusion of prevalent ASCVD at enrollment was based on self-report of myocardial infarction or ischemic stroke, hospitalization records confirming a diagnosis of acute myocardial infarction, ischemic stroke, or their acute complications, or a coronary revascularization procedure.

### *Assessment of atherosclerotic cardiovascular disease risk factors*

Participants completed a detailed questionnaire at enrollment that assessed family history, female reproductive history, smoking history, medication list, immigration history, dietary patterns, activity patterns, psychosocial stressors, household income, and education level. Self-reported data were used to calculate the Townsend Deprivation Index, which is a composite metric of unemployment, lack of car or home ownership, and household overcrowding by geographical area.<sup>43</sup> Anthropometric measurements including height, waist circumference, and hip circumference were measured at the initial enrollment visit. Bioelectrical impedance measurements made by trained staff using hand and foot electrodes on the Tanita BC-418MA body composition analyzer (Tanita, Tokyo, Japan) were used to estimate body and trunk fat mass and percentage, as described elsewhere.<sup>34,35</sup>

Blood work concentrations of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, apolipoprotein A, apolipoprotein B, C-reactive protein, glucose, creatinine, and urea concentrations were assessed at time of enrollment as part of the study protocol. Serum LDL-C concentration was measured using a Beckman Coulter enzymatic selective protection assay, and HDL-C concentration was measured using a Beckman Coulter enzyme immune-inhibition assay, both on a Beckman Coulter AU5800 Platform. Serum triglyceride, urea, glucose, and creatinine concentrations were measured using Beckman Coulter enzymatic assays on a Beckman Coulter AU5800 Platform. Serum cystatin-C concentrations were measured using a Siemens immunoturbidimetric assay on a Siemens Advia 1800 platform. Serum C-reactive protein, apolipoprotein A, and apolipoprotein B concentrations were measured using Beckman Coulter immunoturbidimetric assays on a Beckman Coulter AU5800 Platform. Serum Lp(a) concentrations were measured using a Randox immunoturbidimetric assay using a Beckman Coulter AU5800 Platform. Glycated hemoglobin was measured using high performance liquid chromatography using a Bio-Rad Variant II Turbo Platform.<sup>68</sup>

Diagnosis of hypertension was determined based on self-report, primary care records, or hospitalization records confirming a clinical diagnosis, self-reported consumption of antihypertensive medications, average systolic blood pressure measurement above 140 mm Hg, or average diastolic blood pressure measurement above 90 mm Hg at enrollment. Diagnosis of diabetes was determined based on self-report, primary care records or hospitalization records confirming a clinical diagnosis, self-reported consumption of medications to treat diabetes, or glycated hemoglobin above 6.5% at enrollment. Individuals with a diagnosis of diabetes with glycated hemoglobin greater than 7% were classified as having uncontrolled diabetes. Age at first diagnosis of hypertension and diabetes prior to enrollment were determined from self-report. Chronic kidney disease was defined as glomerular filtration rate less than 60 mL/min/1.73m<sup>2</sup>, as estimated by the CKD-EPI cystatin-C equation.<sup>37</sup> Presence of chronic inflammatory diseases was defined as self-report or hospitalization records confirming a clinical diagnosis of rheumatoid arthritis (ICD9: 714.X; ICD10: M05.X and M06.X), psoriasis or related arthropathy (ICD9: 696.X; ICD10: L40.X, M07.X), lupus erythematosus (ICD9: 695.4; ICD10: L93.X, M32.X), and human immunodeficiency virus infection (ICD10: B20.X-B24.X, R75, Z21.X). Female reproductive factors enhancing cardiovascular disease risk were defined as a

history of menopause prior to age 40, self-report or hospitalization records confirming a clinical diagnosis preterm delivery (ICD10: O60.X), fetus with intrauterine growth retardation (ICD10: O36.5), gestational hypertension (ICD9: 642; ICD10: O13.X), pre-eclampsia (ICD9: 462.7; ICD10: O14.X), eclampsia (ICD10: O15.X), gestational diabetes (ICD10: O24.4), or polycystic ovary syndrome (ICD9: 2564; ICD10: E28.2). Obesity was defined per World Health Organization recommendations as a body mass index  $\geq 27.5$  kg/m<sup>2</sup> in South Asians and  $\geq 30$  kg/m<sup>2</sup> in European ancestry individuals.<sup>38</sup> National Heart, Lung, and Blood obesity (NHLBI) BMI cutoffs of  $\geq 30$  kg/m<sup>2</sup> as obesity in all individuals were used in a comparison analysis.<sup>69</sup> Central adiposity was defined as waist-hip ratio (waist circumference divided by hip circumference) greater than 0.9 in men and greater than 0.85 in women.<sup>39</sup> Waist-height ratio was defined as waist circumference divided by height.

High LDL cholesterol was defined as directly measured concentration above 160 mg/dL (~4.1 mmol/L). Low HDL cholesterol was defined as concentration below 40 mg/dL (~1.0 mmol/L) in men and below 50 mg/dL (~1.3 mmol/L) in women. High triglycerides were defined as concentration above 150 mg/dL (~1.7 mmol/L) for individuals fasting more than 8 hours or above 200 mg/dL (~2.3 mmol/L) for non-fasting individuals. For lipoprotein(a), conversion from nmol/L to mg/dL was performed by dividing by 2.15, as previously described.<sup>70</sup> High lipoprotein(a) was defined as concentration above 50 mg/dL (~107.5 nmol/L). High C-reactive protein was defined as concentration above 3 mg/L.

An unhealthy dietary pattern was ascertained based on a diet score of three or less, computed by assigning one point for adherence to each of the following seven categories: eating at least three pieces of fruit per day, at least nine heaping table-spoons of vegetables per day, at least three servings of whole grains per day, at least two servings of fish per week, no more than 1.5 servings of refined grains and starches a day, no more than one serving of processed meat per week, and no more than 2.5 servings of red meat per week, as previously described.<sup>40,41</sup> Sedentary lifestyle was defined as more than a combined total eight hours a day of the following activities: watching television, sitting in front of a computer, or driving, as previously described.<sup>42</sup> Physical activity frequency, intensity and duration was assessed using adapted questions from the validated International Physical Activity Questionnaire (IPAQ)19.<sup>71</sup> These values were weighted by the expected energy expended for these categories of activity to estimate metabolic equivalent (MET) hours of physical activity for a week, as previously described.<sup>72</sup>

Family history referred to heart disease of any type reported in a first-degree relative at any age. Psychosocial stressors were defined as experiencing any of the following in the two years prior to enrollment: serious illness, injury or assault to self or a relative, death of a close relative or partner, marital separation or divorce, or financial difficulties. Percentage of lifetime spent in the United Kingdom was calculated by subtracting the age at immigration if born abroad (or 0 if born in UK) from age at enrollment, dividing by the age at enrollment, and multiplying by 100. Low household income was defined as an average total pre-tax household income of less than £18,000. Low socioeconomic status was defined as average total pre-tax household income of less than £18,000 or Townsend Deprivation Index—a composite measure of unemployment, household crowding and lack of car or home ownership—in the top decile of the study population ( $\geq 3.41$ ). Highest education level was grouped in order as follows: 1) University or college degree, 2) Advanced level qualifications (A-levels) or equivalent, 3) Ordinary level qualifications (O-levels), General Certificate of Secondary Education (GCSE), Certificate of Secondary Education (CSE) or equivalent, 4) National Vocational Qualifications (NVQ), Higher National Certificate (HNC), Higher National Diploma (HND) or other professional qualifications, or 5) none of the above, as previously described.<sup>73</sup>

#### *Clinical endpoints:*

The primary endpoint was atherosclerotic cardiovascular disease (ASCVD). Incidence of ASCVD was defined based on hospitalization records (ICD9 and ICD10 codes) indicating a diagnosis of acute myocardial infarction, ischemic stroke, or their acute complications, coronary revascularization procedures (coronary artery bypass graft surgery or percutaneous angioplasty/stent placement, OPCS codes), or death register indicating myocardial infarction or ischemic stroke as a cause of death.<sup>44</sup> Coronary artery disease was defined as composite of myocardial infarction and coronary revascularization. Incidence of myocardial infarction was defined based on hospitalization records confirming a diagnosis of acute myocardial infarctions, its acute complications, or death

register indicating ischemic heart disease as a cause of death. Incidence of coronary revascularization was defined based on hospitalization records confirming a coronary revascularization procedure (coronary artery bypass graft surgery or percutaneous angioplasty/stent placement). Incidence of ischemic stroke was defined based on hospitalization records confirming a diagnosis of acute ischemic stroke (cerebral infarction due to thrombosis or cerebral atherosclerosis or cerebrovascular syndromes), its acute complications, or death register indicating ischemic stroke as a cause of death. Nonfatal outcomes were ascertained based on hospitalization and procedural records while fatal outcomes were ascertained from death registry data.

Additional cardiovascular endpoints were also examined. Incidence of heart failure was defined based on hospitalization records indicating any diagnosis of congestive heart failure, left heart failure, or cardiomyopathy. Incidence of atrial fibrillation or flutter was defined as diagnosis of atrial fibrillation or atrial flutter or related ablation procedures. Incidence of peripheral artery disease was defined as hospitalization records indicating atherosclerosis of peripheral arteries or procedures involving endarterectomy, angioplasty, stenting, or bypass of peripheral arteries

#### *ICD and OPCS codes for risk factors and endpoints*

##### *Hypertension:*

*ICD 9:* 401, 4010, 4011, 4019, 402, 4020, 4021, 4029, 403, 4031, 4039, 404, 4040, 4041, 4049, 405, 4050, 4051, 4059

*ICD 10:* I10, I11, I11.0, I11.9, I12, I12.0, I12.9, I13, I13.0, I13.1, I13.2, I13.9, I15, I15.0, I15.1, I15.2, I15.8, I15.9

##### *Type 2 diabetes mellitus:*

*ICD 9:* 2500, 25000, 25001, 25009, 25011, 25019, 2503, 2504, 2505, 25099

*ICD 10:* E10, E10.1, E10.2, E10.3, E10.4, E10.5, E10.6, E10.7, E10.8, E10.9, E11, E11.0, E11.1, E11.2, E11.3, E11.4, E11.5, E11.6, E11.7, E11.8, E11.9, E12, E12.1, E12.8, E12.9, E13, E13.1, E13.2, E13.3, E13.5, E13.6, E13.7, E13.8, E13.9, E14, E14.1, E14.2, E14.3, E14.4, E14.5, E14.6, E14.7, E14.8, E14.9

##### *Atherosclerotic cardiovascular disease:*

*ICD9:* 410, 4109, 411, 4119, 412, 4129, 433, 434, 4331, 4339, 4349, 4359, 4369, 4370, 4371, 4378, 4379, 4389

*ICD10:* G45, G45.0, G45.1, G45.3, G45.4, G45.8, G45.9, G46, G46.3, G46.4, G46.5, G46.7, G46.8, I63, I63.0, I63.2, I63.3, I63.5, I63.8, I63.9, I64, I65, I65.0, I65.1, I65.2, I65.3, I65.8, I65.9, I66, I66.0, I66.1, I66.2, I66.3, I66.4, I66.8, I66.9, I67.2, I69.4, I21, I21.0, I21.1, I21.2, I21.3, I21.4, I21.9, I22, I22.0, I22.1, I22.8, I22.9, I23, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24, I24.0, I24.1, I24.8, I24.9, I25.2

*OPCS4:* K40, K40.1, K40.2, K40.3, K40.4, K40.8, K40.9, K41, K41.1, K41.2, K41.3, K41.4, K41.8, K41.9, K42, K42.1, K42.2, K42.3, K42.4, K42.8, K42.9, K43, K43.1, K43.2, K43.3, K43.4, K43.8, K43.9, K44, K44.1, K44.2, K44.8, K44.9, K45.1, K45.2, K45.3, K45.4, K45.5, K45.6, K45.8, K45.9, K46, K46.1, K46.2, K46.3, K46.4, K46.5, K46.8, K46.9, K49.1, K49.2, K49.3, K49.4, K49.8, K49.9, K50.1, K50.2, K50.4, K75.1, K75.2, K75.3, K75.4, K75.8, K75.9

##### *Coronary artery disease:*

*ICD 9:* 410, 4109, 411, 4119, 412, 4129

*ICD10:* I21, I21.0, I21.1, I21.2, I21.3, I21.4, I21.9, I22, I22.0, I22.1, I22.8, I22.9, I23, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24, I24.0, I24.1, I24.8, I24.9, I25.2

*OPCS4:* K40, K40.1, K40.2, K40.3, K40.4, K40.8, K40.9, K41, K41.1, K41.2, K41.3, K41.4, K41.8, K41.9, K42, K42.1, K42.2, K42.3, K42.4, K42.8, K42.9, K43, K43.1, K43.2, K43.3, K43.4, K43.8, K43.9, K44, K44.1, K44.2, K44.8, K44.9, K45.1, K45.2, K45.3, K45.4, K45.5, K45.6, K45.8, K45.9, K46, K46.1, K46.2, K46.3, K46.4, K46.5, K46.8, K46.9, K49.1, K49.2, K49.3, K49.4, K49.8, K49.9, K50.1, K50.2, K50.4, K75.1, K75.2, K75.3, K75.4, K75.8, K75.9

##### *Myocardial infarction:*

*ICD 9:* 410, 4109, 411, 4119, 412, 4129

*ICD10:* I21, I21.0, I21.1, I21.2, I21.3, I21.4, I21.9, I22, I22.0, I22.1, I22.8, I22.9, I23, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24, I24.0, I24.1, I24.8, I24.9, I25.2

##### *Coronary revascularization:*

*OPCS4:* K40, K40.1, K40.2, K40.3, K40.4, K40.8, K40.9, K41, K41.1, K41.2, K41.3, K41.4,

K41.8,K41.9,K42,K42.1,K42.2,K42.3,K42.4,K42.8,K42.9,K43,K43.1,K43.2,K43.3,  
K43.4,K43.8,K43.9,K44,K44.1,K44.2,K44.8,K44.9,K45.1,K45.2,K45.3,K45.4,K45.5,  
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K49.3,K49.4,K49.8,K49.9,K50.1,K50.2,K50.4,K75.1,K75.2,K75.3,K75.4,K75.8,K75.9

#### Ischemic stroke:

*ICD9*:433,434,4331,4339,4349,4359,4369,4370,4371,4378,4379,4389

*ICD10*:G45,G45.0,G45.1,G45.3,G45.4,G45.8,G45.9,G46,G46.3,G46.4,G46.5,G46.7,G46.8,I6  
3,I63.0,I63.2,I63.3,I63.5,I63.8,I63.9,I64,I65,I65.0,I65.1,I65.2,I65.3,I65.8,I65.9,I66,I66.0,I66.  
1,I66.2,I66.3,I66.4,I66.8,I66.9,I67.2,I69.4

#### Atrial fibrillation or flutter

*ICD9*: 4273

*ICD10*: I48,I48.0,I48.1,I48.2,I48.3,I48.4,I48.9

*OPCS4*: K57.1,K62.1,K62.2,K62.3,K62.4,X50.1,X50.2

#### Heart failure:

*ICD9*: 4254,4280,4281

*ICD10*:I11.0,I13.0,I13.2,I25.5,I42.0,I42.1,I42.2,I42.5,I42.8,I42.9,I50,I50.0,I50.1,I50.9

#### Peripheral artery disease:

*ICD9*: 4400,4401,4402,4408,4409,4438,4439

*ICD10*:

I70.1,I70.11,I70.0,I70.00,I70.01 ,I70.2,I70.20,I70.21,I70.8,I70.80,I70.9,I70.90,I70.91,I73.8,I  
73.9

*OPCS4*:

L162,L163,L216 ,L251,L252,L293,L294,L295,L297,L311,L314,L371,L372,L373,L374,L391  
,L395,L412,L414,L431,L435,L451,L453,L454,L471,L474,L511,L512,L513,L514,L515,L516  
,L518 ,L518,L521,L522,L541,L544,L548,L591,L592,L593,L594,L595,L596,L597,L598,L59  
9,L601,L602,L603,L604,L608,L609,L631,L635,L665,L667,L681,L682,L711,L717,X093,X0  
94,X095

#### Statistical analysis

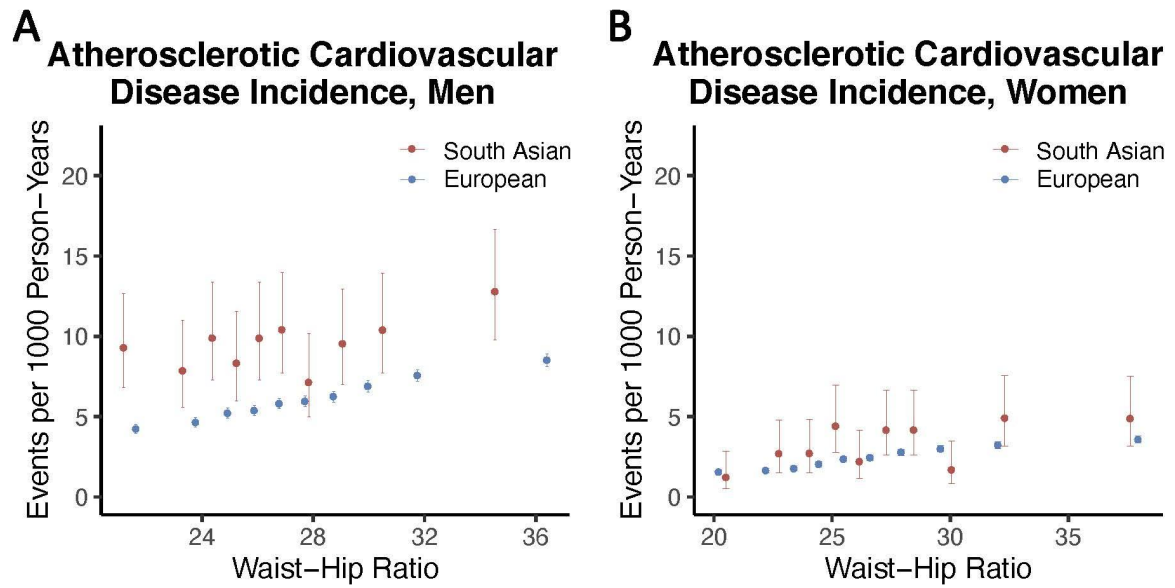
All statistical analyses were performed with the use of R software, version 3.5 (R Project for Statistical Computing). Comparison of baseline characteristics between individuals of subgroups of South Asian versus European ancestry was performed with the chi-squared test for categorical variables, analysis of variance (ANOVA) for continuous variables, and Mann-Whitney U test for continuous variables with nonparametric distributions. Standardized mean differences were estimated using the ‘tableone’ package in R, and a difference of less than 0.1 was taken to indicate a negligible difference in the mean or prevalence of a variable between ancestry groups.<sup>45,46</sup> The ACC/AHA Pooled Cohort Equations and the QRISK3 Equations were used to predict the 10-year risk estimates for subgroup of individuals of South Asian and European ancestry without prior ASCVD noted in primary care, hospitalization, or procedural records or statin use.<sup>9,47,48</sup> Risk for incident ASCVD for South Asian relative to European ancestry was calculated using Cox proportional hazards regression models, including covariates of age, sex, enrollment center, and self-reported ancestry. ASCVD incidence rates were estimated as events per 1000 person-years of follow up time and adjusted for age and sex using Poisson regression and the ‘epiR’ package in R.<sup>49,50</sup> Individuals were binned into deciles according to waist-hip ratio, and unadjusted incidence rates of ASCVD were determined within each decile bin, stratified by ancestry and sex.

Risk for development of incident ASCVD after enrollment associated with a given risk factor category was computed using Cox proportional hazards regression models for each ancestry, including covariates of age, sex, enrollment center, and risk factor of interest. Proportion of disease variance explained in each ancestry was calculated for each risk factor group using Nagelkerke’s pseudo- $R^2$  metric, as previously described.<sup>51</sup> The change in  $R^2$  was calculated for the model inclusive of the risk factor group of interest plus the covariates of age, sex, and enrollment center minus  $R^2$  for the covariates alone, thus yielding an estimate of the explained variance. Ancestry specific  $R^2$  estimates were also computed for each risk factor stratified by sex. Bootstrapping was performed 200 times for the estimation of 95% confidence intervals for each of these estimates. Prior diagnosis of hypertension, systolic blood pressures, and diastolic blood pressures were grouped as hypertension

measures. Prior diagnosis of diabetes and glycated hemoglobin concentrations were grouped as diabetes measures. Body mass index and body fat percentage derived from bioelectrical impedance measurements were grouped as obesity measures. Waist-hip ratio and trunk fat percentage derived from bioelectrical impedance measurements were grouped as central adiposity measures. Townsend Deprivation Index and average household income were grouped as socioeconomic measures. Triglyceride, lipoprotein(a), and C-reactive protein concentrations were log-transformed prior to inclusion in statistical models. Population attributable fractions for each risk factor were calculated and compared among individuals stratified by ancestry and sex using categorized risk factors using the 'epiR' package in R.<sup>50</sup>

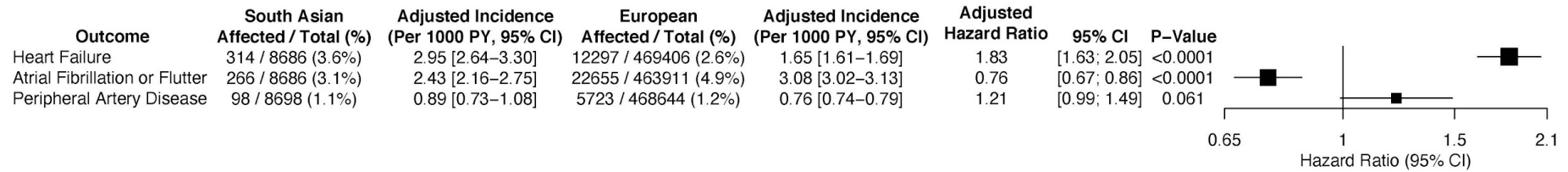
Available outpatient records were examined to help assess healthcare utilization and risk factor control over time in the follow-up period. Number of primary care visits in the follow-up period were determined by summing the number of unique dates of logged general practitioner visits after the enrollment date. Time weighted average estimates of LDL cholesterol, glycated hemoglobin, systolic blood pressure, and diastolic blood pressure were determined by multiplying each value measured after enrollment by the number of days from midway between prior and current measurements to midway between current and next measurements, summing these weighted values, and then dividing by the total number of days of follow-up. Sensitivity analyses were performed using time-weighted outpatient risk factor values in place of measurements taken during enrollment visit. The extent to which the higher risk for incident ASCVD in South Asian versus European ancestry individuals was associated with traditional and emerging risk factors was assessed using a baseline Cox proportional hazard models with age, sex, and enrollment center as covariates, followed by sequential addition of additional risk factor groups of interest into the model. For these Cox proportional hazards regressions models, individuals missing data for any covariate in the model of interest were excluded from that analysis. Additional mediation analysis was performed to evaluate the proportional association of each risk factor to the association between ancestry and atherosclerotic cardiovascular disease risk using the 'mediation' package in R.<sup>52</sup> Each mediator model was adjusted for age, sex, enrollment center and each of the risk factor variables not under consideration. Each incident cardiovascular outcome survival model was adjusted for age, sex, enrollment center, and all the risk factor variable of interest. Each mediation analysis model was run using 1,000 simulations with a quasi-Bayesian approach to estimate variance.

**Figure I:** Incidence of atherosclerotic cardiovascular disease according to waist-hip ratio



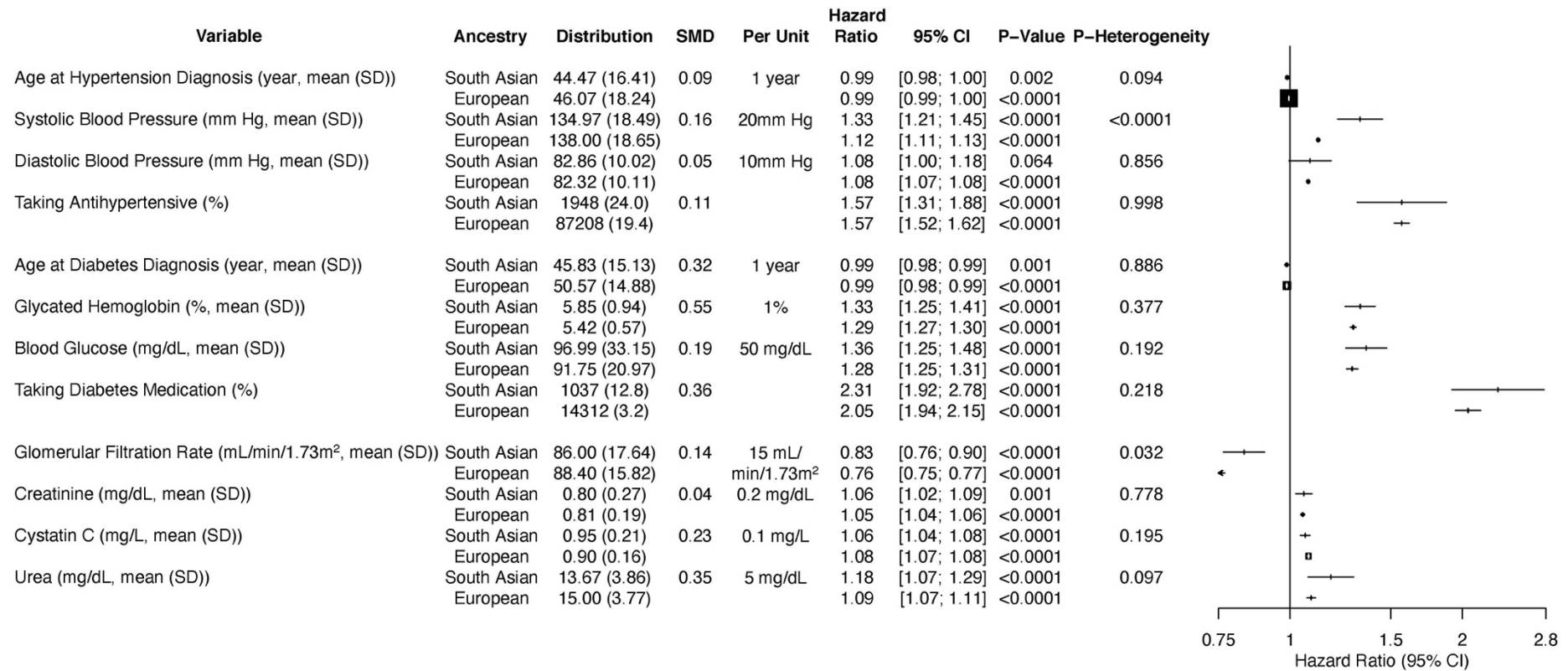
Unadjusted incidence rates per 1000 person-years with corresponding 95% confidence intervals of atherosclerotic cardiovascular disease events grouped by deciles of the waist-hip ratio distribution stratified by ancestry for **A**: men and **B**: women.

**Figure II:** Adjusted hazard ratios of additional cardiovascular disease endpoints for South Asians relative to individuals of European ancestry



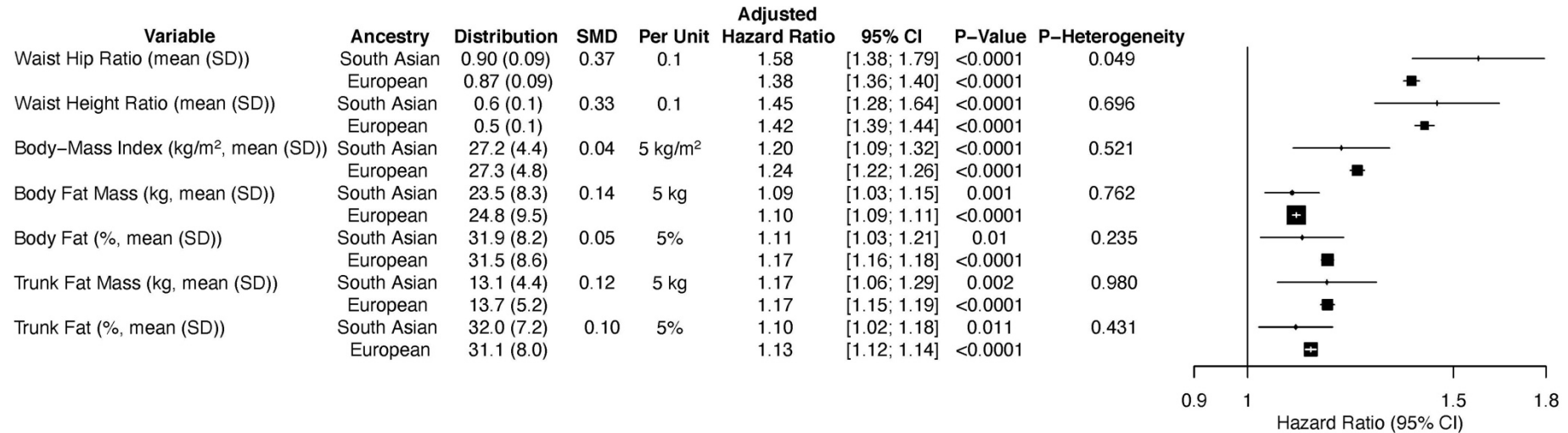
Adjusted hazard ratios with corresponding 95% confidence intervals and p values for heart failure, atrial fibrillation, and peripheral artery disease endpoints, comparing individuals of South Asian ancestry to individuals of European ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center. Adjusted incidence rates estimated as events per 1000 person-years (PY) of follow up time and adjusted for age and sex using Poisson regression.

**Figure III:** Distributions and adjusted hazard ratios for atherosclerotic cardiovascular disease for comorbidity variables



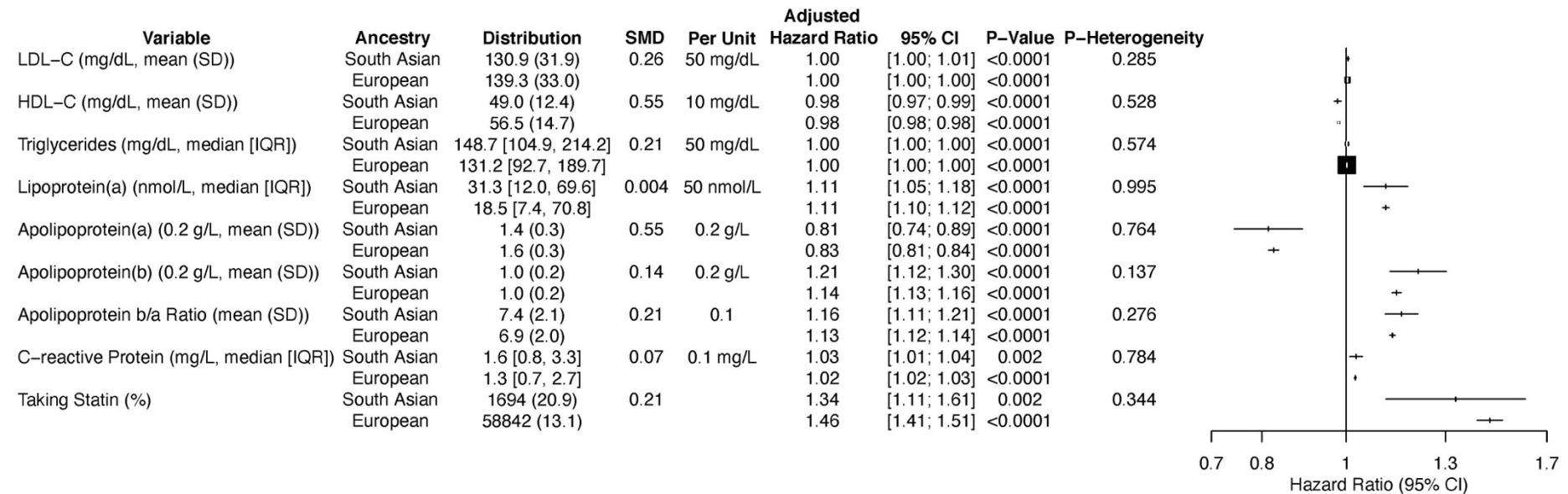
Distributions and adjusted hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease risk imparted by variable of interest, stratified by ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center. Distribution P-value compares variable distribution between ancestry groups. Hazard ratios and P-values are estimated per listed unit increments if continuous variable or for presence of a categorical variable. Standardized mean differences (SMD) compare ancestry-specific distributions of risk factor and a value >0.1 is deemed to be significant. P-heterogeneity compares hazard ratios between ancestry groups and is deemed significant if <0.05.

**Figure IV:** Distributions and adjusted hazard ratios for atherosclerotic cardiovascular disease for anthropometric variables



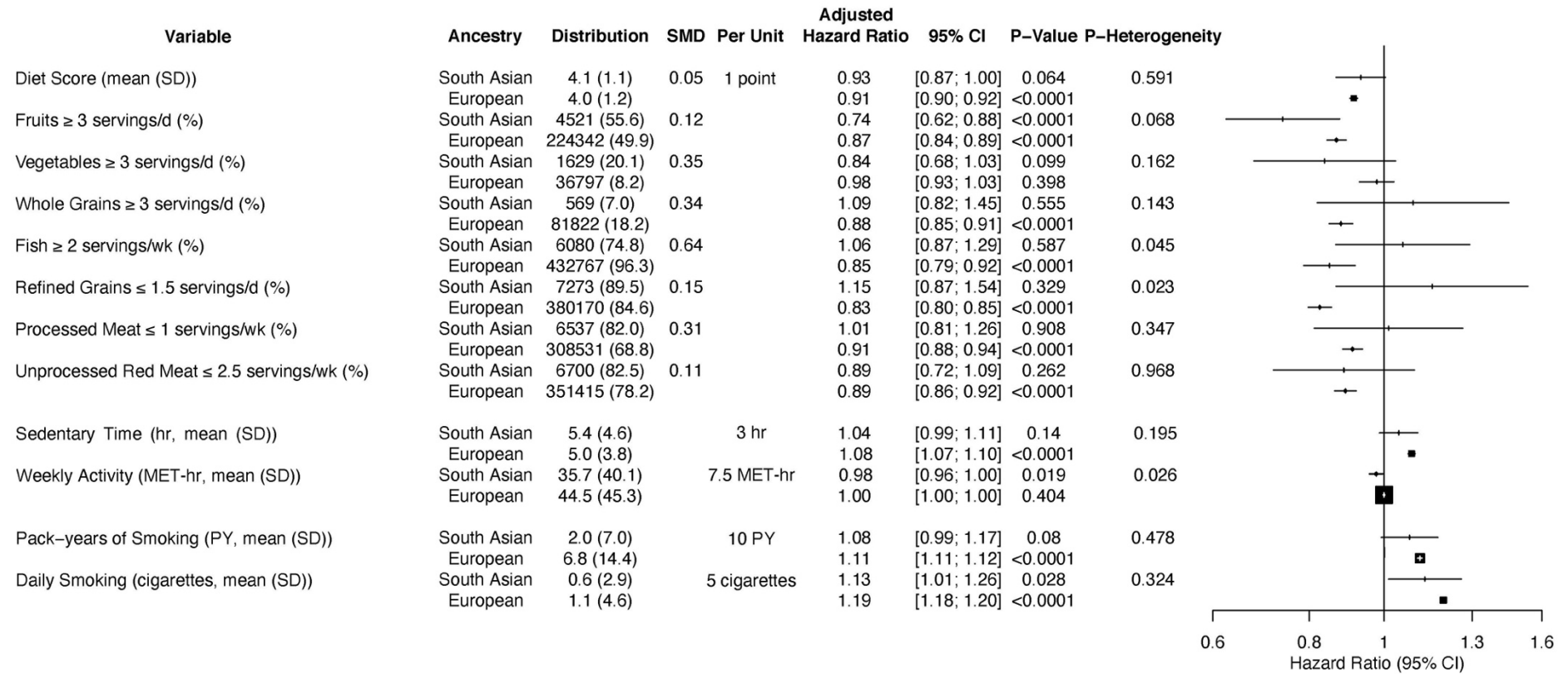
Distributions and adjusted hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease risk imparted by variable of interest, stratified by ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center. Distribution P-value compares variable distribution between ancestry groups. Hazard ratios and P-values are estimated per listed unit increments if continuous variable or for presence of a categorical variable. Standardized mean differences (SMD) compare ancestry-specific distributions of risk factor and a value >0.1 is deemed to be significant. P-heterogeneity compares hazard ratios between ancestry groups and is deemed significant if <0.05.

**Figure V:** Distributions and adjusted hazard ratios for atherosclerotic cardiovascular disease for lipid and inflammation-related variables



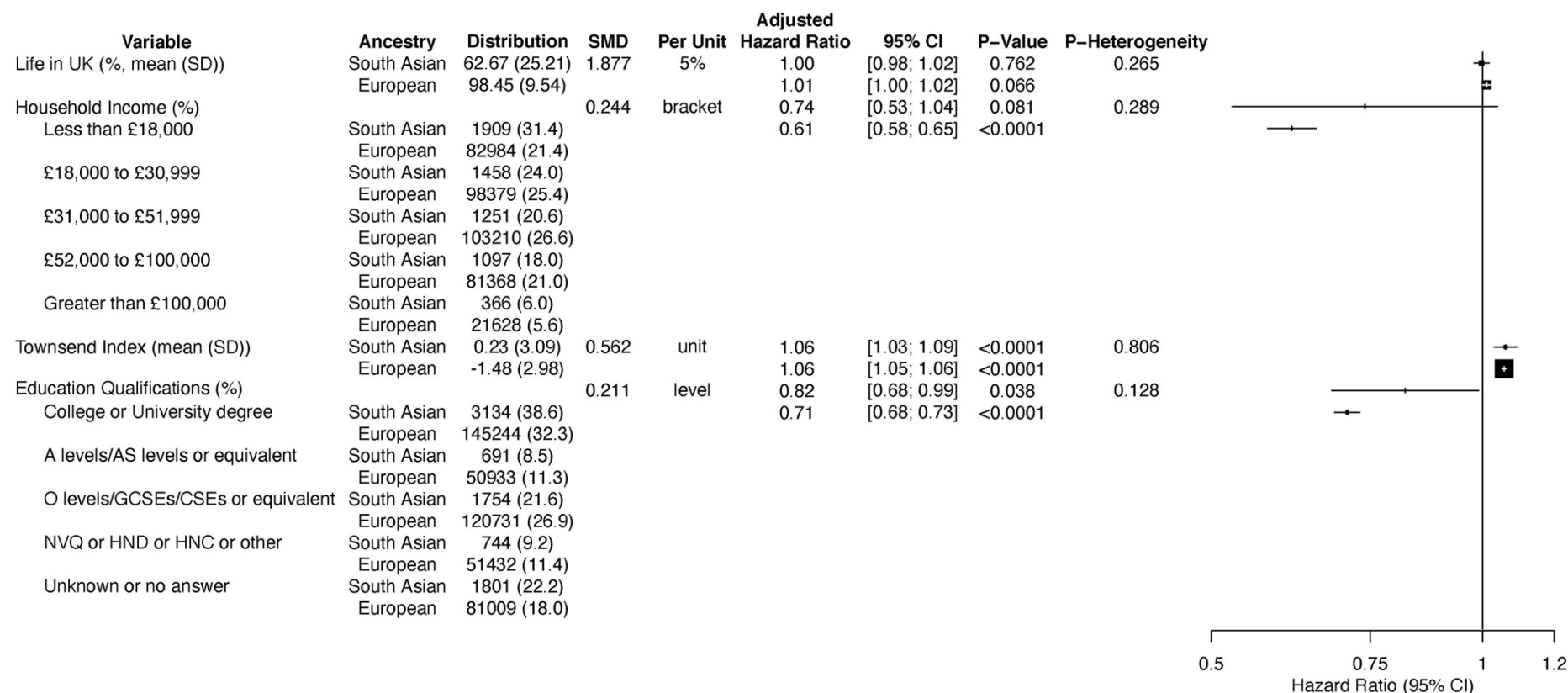
Distributions and adjusted hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease risk imparted by variable of interest, stratified by ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center. Distribution P-value compares variable distribution between ancestry groups. Hazard ratios and P-values are estimated per listed unit increments if continuous variable or for presence of a categorical variable. Standardized mean differences (SMD) compare ancestry-specific distributions of risk factor and a value >0.1 is deemed to be significant. P-heterogeneity compares hazard ratios between ancestry groups and is deemed significant if <0.05. LDL: Low-density lipoprotein. HDL: High-density lipoprotein.

**Figure VI:** Distributions and adjusted hazard ratios for atherosclerotic cardiovascular disease for lifestyle variables



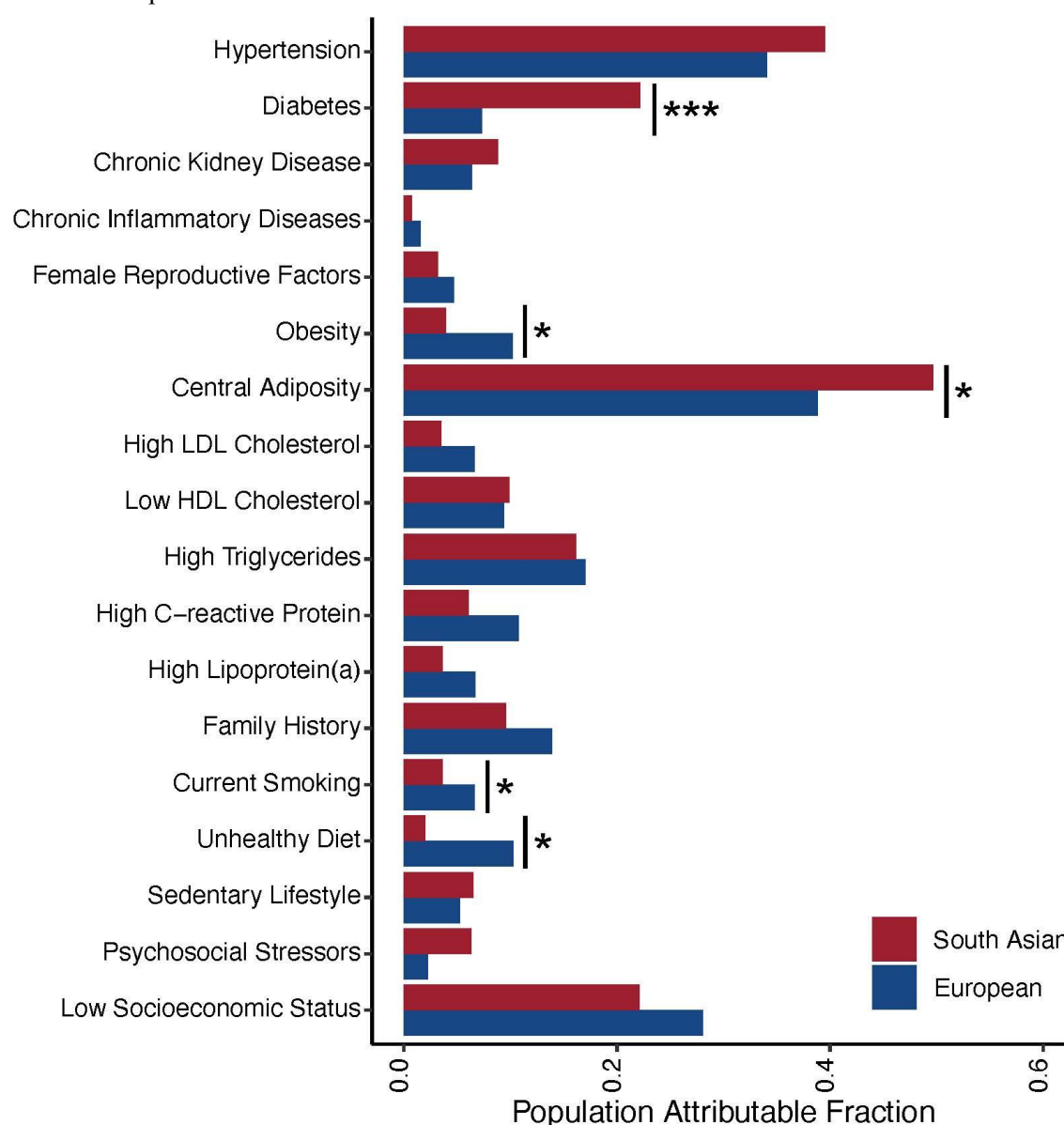
Distributions and adjusted hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease risk imparted by variable of interest, stratified by ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center. MET-hr: metabolic equivalent of task hour. PY: pack-year. Distribution P-value compares variable distribution between ancestry groups. Hazard ratios and P-values are estimated per listed unit increments if continuous variable or for presence of a categorical variable. Standardized mean differences (SMD) compare ancestry-specific distributions of risk factor and a value >0.1 is deemed to be significant. P-heterogeneity compares hazard ratios between ancestry groups and is deemed significant if <0.05.

**Figure VII:** Distributions and adjusted hazard ratios for atherosclerotic cardiovascular disease for socioeconomic variables



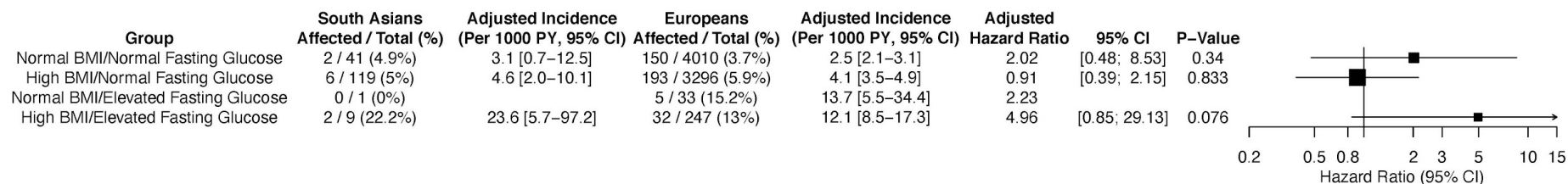
Distributions and adjusted hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease risk imparted by variable of interest, stratified by ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center. Distribution P-value compares variable distribution between ancestry groups. Hazard ratios and P-values are estimated per listed unit increments if continuous variable or for presence of a categorical variable. Standardized mean differences (SMD) compare ancestry-specific distributions of risk factor and a value >0.1 is deemed to be significant. P-heterogeneity compares hazard ratios between ancestry groups and is deemed significant if <0.05. A-levels: Advanced level qualifications (A-levels). O-levels: Ordinary level qualifications. GCSE: General Certificate of Secondary Education. CSE: Certificate of Secondary Education. NVQ: National Vocational Qualifications. HND: Higher National Diploma. HNC: Higher National Certificate.

**Figure VIII:** Population attributable fractions of atherosclerotic cardiovascular disease risk



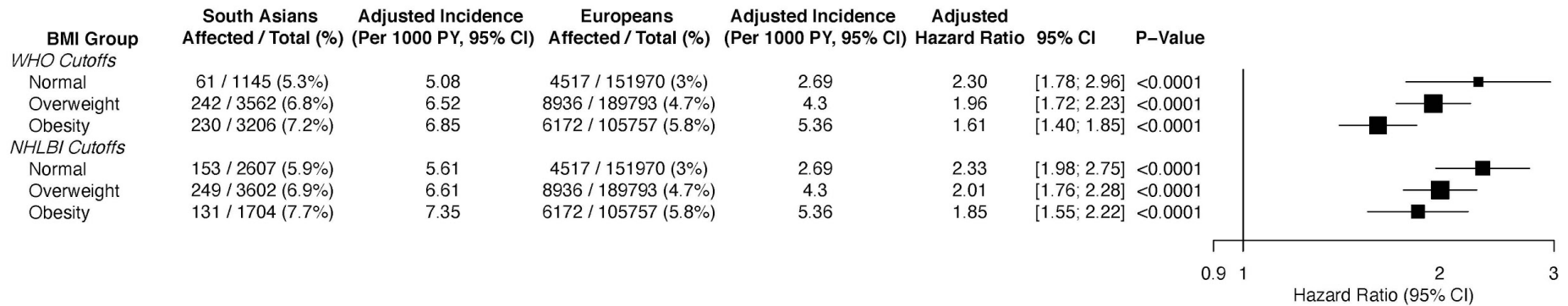
Population attributable fractions for atherosclerotic cardiovascular disease risk factors stratified by ancestry. Statistically significant differences in estimated fractions for two ancestries denoted by \*\*\* for p-value < 0.001 and \* for p-value < 0.05 (Supplemental Table 3). LDL: Low-density lipoprotein. HDL: High-density lipoprotein. Chronic kidney disease: glomerular filtration rate less than 60 mL/min/1.73m<sup>2</sup>. Female reproductive factors: history of menopause before age 40, preterm delivery, fetus with intrauterine growth retardation, gestational hypertension, pre-eclampsia, eclampsia, gestational diabetes, or polycystic ovary syndrome. Chronic inflammatory diseases: rheumatoid arthritis, psoriasis, lupus erythematosus, or human immunodeficiency virus infection.

**Figure IX:** Adjusted hazard ratios for atherosclerotic cardiovascular disease for South Asians relative to individuals of European ancestry stratified by body mass index cut-offs and fasting glucose levels



Hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease, comparing individuals of South Asian ancestry to individuals of European ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center, stratified by body mass index (BMI) and fasting glucose category. High BMI:  $\geq 27.5$  kg/m<sup>2</sup> for South Asians and  $\geq 30$  kg/m<sup>2</sup> for European ancestry individuals. Normal BMI:  $< 23$  kg/m<sup>2</sup> for South Asians and  $< 25$  kg/m<sup>2</sup> for European ancestry individuals. Elevated fasting glucose:  $\geq 126$  mg/dL in individuals fasting more than 8 hours at time of blood draw. Normal fasting glucose:  $< 100$  mg/dL in individuals fasting more than 8 hours at time of blood draw. Adjusted incidence rates estimated as events per 1000 person-years (PY) of follow up time and adjusted for age and sex using Poisson regression.

**Figure X:** Adjusted hazard ratios for atherosclerotic cardiovascular disease for South Asians relative to individuals of European ancestry stratified by body mass index categories



Hazard ratios with corresponding 95% confidence intervals and p values for atherosclerotic cardiovascular disease, comparing individuals of South Asian ancestry to individuals of European ancestry, calculated using Cox proportional hazards regression models with covariates of enrollment age, sex, and testing center, stratified by body mass index (BMI) categories. World Health Organization cut-offs for BMI for South Asians are: Normal BMI:  $<23 \text{ kg/m}^2$ ; overweight:  $\text{BMI} \geq 23 \text{ kg/m}^2$  but  $<27.5 \text{ kg/m}^2$ ; obese:  $\text{BMI} \geq 27.5 \text{ kg/m}^2$ . World Health Organization cut-offs for BMI for European ancestry individuals and National Heart, Lung, and Blood Institute (NHLBI) BMI cut-offs for both ancestries are: Normal BMI:  $<25 \text{ kg/m}^2$ ; overweight:  $\text{BMI} \geq 25 \text{ kg/m}^2$  but  $<30 \text{ kg/m}^2$ ; obese:  $\text{BMI} \geq 30 \text{ kg/m}^2$ . Adjusted incidence rates estimated as events per 1000 person-years (PY) of follow up time and adjusted for age and sex using Poisson regression.

**Table I:** Missing data in risk factor variables of main analyses

	European (n=449,349)		South Asian (n=8,124)		Total (n=457,743)	
	N Missing	% Missing	N Missing	% Missing	N Missing	% Missing
Hypertension Measures						
Hypertension Diagnosis	0	0	0	0	0	0
Systolic Blood Pressure	702	0.16	47	0.58	749	0.16
Diastolic Blood Pressure	700	0.16	47	0.58	747	0.16
Blood Pressure Medication	0	0	0	0	0	0
Diabetes Measures						
Diabetes Diagnosis	0	0	0	0	0	0
Glycated Hemoglobin	28,695	6.39	752	9.26	29,447	6.44
Diabetes Medication	0	0	0	0	0	0
Glomerular Filtration Rate	27,403	6.1	633	7.79	28,036	6.13
Chronic Inflammatory Diseases	2,354	0.52	45	0.55	2,399	0.52
Female Reproductive Factors (totals for women)	0	0	0	0	0	0
Obesity Measures						
Body Mass Index	1,829	0.41	211	2.6	2,040	0.45
Body Fat Percentage	7,615	1.69	203	2.5	7,818	1.71
Central Adiposity Measures						
Waist-Hip Ratio	1,331	0.3	108	1.33	1,439	0.31
Trunk Fat Percentage	7,639	1.7	205	2.52	7,844	1.71
LDL Cholesterol	28,102	6.25	647	7.96	28,749	6.28
HDL Cholesterol	62,086	13.82	1,284	15.81	63,370	13.85
Triglycerides	27,690	6.16	641	7.89	28,331	6.19
Lipoprotein(a)	36,754	8.18	778	9.58	37,532	8.2
C-reactive Protein	28,227	6.28	659	8.11	28,886	6.31

Family History of Heart Disease	0	0	0	0	0	0
Current Smoking	1,427	0.32	90	1.11	1,517	0.33
Diet Score	9,521	2.12	690	8.49	10,211	2.23
Sedentary Lifestyle	12,775	2.84	922	11.35	13,697	2.99
Psychosocial Stressors	4,817	1.07	369	4.54	5,186	1.13
Socioeconomic Measures						
Townsend Deprivation Index	537	0.12	9	0.11	546	0.12
Household Income	61,780	13.75	2,043	25.15	63,823	13.95
<i>All Variable Groups</i>	99,042	22.04	2,846	35.03	101,888	22.27

Summary of missing variables from main analyses of individuals studied in the UK Biobank. For variables tabulated from ICD codes, the absence of associated ICD codes in chart was coded as absence of risk factor and not missing. LDL: Low-density lipoprotein. HDL: High-density lipoprotein. Chronic kidney disease: glomerular filtration rate less than 60 mL/min/1.73m<sup>2</sup>. Female reproductive factors: history of menopause before age 40, preterm delivery, fetus with intrauterine growth retardation, gestational hypertension, pre-eclampsia, eclampsia, gestational diabetes, or polycystic ovary syndrome. Chronic inflammatory diseases: rheumatoid arthritis, psoriasis, lupus erythematosus, or human immunodeficiency virus infection. Body fat percentage and trunk fat percentage estimated using bioelectrical impedance measures.

**Table II:** Baseline characteristics of individuals of European ancestry and South Asian ancestry subgroup

	European	Indian	Pakistani	Bangladeshi	Other South Asian	P-Value	SMD
n	449349	5554	1669	211	690		
Male Sex (%)	198210 (44.1)	2693 (48.5)	976 (58.5)	140 (66.4)	386 (55.9)	<0.001	0.22
PCE 10yr Risk (%; median [IQR])	6.0 [2.6, 12.0]	4.8 [2.0, 10.8]	4.3 [2.0, 9.9]	4.7 [1.9, 8.9]	5.7 [2.6, 13.0]	<0.001	0.09
QRISK3 10 yr Risk (%; median [IQR])	8.3 [4.0, 14.7]	9.4 [4.2, 18.3]	11.4 [5.6, 22.7]	9.5 [5.3, 18.6]	8.7 [4.1, 16.5]	<0.001	0.23
Hypertension (%)	174139 (38.8)	2383 (42.9)	631 (37.8)	73 (34.6)	310 (44.9)	<0.001	0.11
Taking Blood Pressure Medication (%)	87208 (19.4)	1393 (25.1)	337 (20.2)	42 (19.9)	176 (25.5)	<0.001	0.08
Diabetes (%)	23733 (5.3)	979 (17.6)	388 (23.2)	63 (29.9)	156 (22.6)	<0.001	0.30
Taking Diabetes Medication (%)	14312 (3.2)	642 (11.6)	256 (15.3)	43 (20.4)	96 (13.9)	<0.001	0.25
Chronic Kidney Disease (%)	17689 (4.2)	439 (8.5)	93 (6.1)	17 (9.0)	30 (4.7)	<0.001	0.11
Chronic Inflammatory Diseases (%)	16420 (3.7)	222 (4.0)	64 (3.9)	9 (4.3)	18 (2.6)	0.35	0.04
Female Reproductive Factors (%)	25096 (5.6)	286 (5.1)	103 (6.2)	11 (5.2)	28 (4.1)	0.187	0.04
Body Mass Index (kg/m <sup>2</sup> ; mean (SD))	27.3 (4.8)	26.9 (4.3)	28.4 (4.7)	26.2 (3.7)	26.6 (3.8)	<0.001	0.24
Waist-hip Ratio (mean (SD))	8.68 (0.89)	8.93 (0.86)	9.16 (0.83)	9.20 (0.73)	9.16 (0.81)	<0.001	0.30
LDL Cholesterol (mg/dL; mean (SD))	139.3 (33.0)	131.1 (31.7)	129.9 (31.4)	127.3 (33.1)	132.9 (34.0)	<0.001	0.17
HDL Cholesterol (mg/dL; mean (SD))	56.5 (14.7)	50.2 (12.5)	45.5 (11.0)	43.7 (12.0)	49.0 (12.9)	<0.001	0.47
Triglycerides (mg/dL; median [IQR])	131.2 [92.7, 189.6]	145.6 [103.5, 208.9]	158.3 [111.9, 223.5]	155.3 [102.5, 251.1]	154.2 [102.7, 225.6]	<0.001	0.17
Lipoprotein(a) (nmol/L; median [IQR])	18.5 [7.4, 70.8]	32.2 [12.1, 71.2]	27.7 [11.6, 62.7]	25.4 [9.1, 56.7]	33.1 [12.2, 75.9]	<0.001	0.12
C-reactive Protein (mg/L; median [IQR])	0.3 (1.1)	0.5 (1.0)	0.7 (1.0)	0.5 (1.0)	0.3 (1.0)	<0.001	0.19

Taking Statin (%)	58842 (13.1)	1133 (20.4)	330 (19.8)	54 (25.6)	177 (25.7)	<0.001	0.16
Family History of Heart Disease (%)	196462 (43.7)	2305 (41.5)	737 (44.2)	68 (32.2)	247 (35.8)	<0.001	0.13
Current Smoking (%)	46373 (10.4)	390 (7.1)	204 (12.4)	54 (26.1)	58 (8.5)	<0.001	0.24
Unhealthy Diet (%)	136506 (30.4)	1363 (24.5)	608 (36.4)	86 (40.8)	203 (29.4)	<0.001	0.17
Sedentary Lifestyle (%)	53307 (12.2)	795 (15.9)	281 (19.7)	30 (17.1)	103 (16.8)	<0.001	0.09
Psychosocial Stressors (%)	193873 (43.6)	2676 (50.0)	918 (59.6)	111 (57.5)	308 (46.0)	<0.001	0.18
Townsend Deprivation Index (mean (SD))	-1.5 (3.0)	-0.2 (2.9)	1.3 (3.2)	2.9 (3.7)	0.1 (3.1)	<0.001	0.62
Household Income (%)						<0.001	0.47
Less than £18,000	82984 (21.4)	1062 (25.4)	586 (48.7)	85 (60.7)	176 (32.1)		
£18,000 to £30,999	98379 (25.4)	1050 (25.1)	246 (20.4)	17 (12.1)	145 (26.4)		
£31,000 to £51,999	103210 (26.6)	935 (22.3)	183 (15.2)	22 (15.7)	111 (20.2)		
£52,000 to £100,000	81368 (21.0)	852 (20.3)	139 (11.6)	14 (10.0)	92 (16.8)		
Greater than £100,000	21628 (5.6)	290 (6.9)	49 (4.1)	2 (1.4)	25 (4.6)		

Summary of baseline characteristics of individuals studied in the UK Biobank. PCE: American Heart Association/American College of Cardiology Pooled Cohort Equations. LDL: Low-density lipoprotein. HDL: High-density lipoprotein. Chronic kidney disease: glomerular filtration rate less than 60 mL/min/1.73m<sup>2</sup>. Female reproductive factors: history of menopause before age 40, preterm delivery, fetus with intrauterine growth retardation, gestational hypertension, pre-eclampsia, eclampsia, gestational diabetes, or polycystic ovary syndrome. Chronic inflammatory diseases: rheumatoid arthritis, psoriasis, lupus erythematosus, or human immunodeficiency virus infection. P-value is deemed significant if <0.05. Standardized mean differences (SMD) compare ancestry-specific distributions of risk factor and a value >0.1 is deemed to be significant.

**Table III:** Proportion of variance in atherosclerotic cardiovascular disease risk associated with risk factor group

	Proportion of Variance Explained (SD)	
	European	South Asian
Hypertension and Blood Pressure	0.0037 (0.0002)	0.0102 (0.0022)
Diabetes and Glycated Hemoglobin	0.0024 (0.0002)	0.0082 (0.0028)
Glomerular Filtration Rate	0.0030 (0.0002)	0.0024 (0.0017)
Chronic Inflammatory Diseases	0.0001 (0.0001)	0.0005 (0.0005)
Female Reproductive Factors	0.0001 (0.000)	0.0003 (0.0003)
Obesity Measures	0.0017 (0.0002)	0.0016 (0.0014)
Central Adiposity Measures	0.0025 (0.0002)	0.0059 (0.0019)
LDL Cholesterol	0.0004 (0.0001)	0.0011 (0.0016)
HDL Cholesterol	0.0025 (0.0002)	0.0041 (0.0024)
Triglycerides	0.0019 (0.0002)	0.0034 (0.0017)
Lipoprotein(a)	0.0011 (0.0002)	0.0013 (0.0015)
C-reactive Protein	0.0024 (0.0002)	0.0012 (0.0017)
Family History of Heart Disease	0.0010 (0.0001)	0.0013 (0.0007)
Current Smoking	0.0018 (0.0001)	0.0004 (0.0008)
Diet Score	0.0005 (0.0001)	0.0006 (0.0005)
Sedentary Time	0.0005 (0.0001)	-0.0005 (0.0015)
Psychosocial Stressors	0.0004 (0.0001)	0.0012 (0.0010)
Socioeconomic Measures	0.0018 (0.0002)	0.0027 (0.0025)

Proportion of variance explained was calculated for each disease using Nagelkerke's pseudo-R<sup>2</sup> metric. The R<sup>2</sup> was calculated for the full model inclusive of the risk factor group of interest plus the baseline covariates (age at enrollment, sex, and enrollment center) minus R<sup>2</sup> for the baseline covariates alone, thus yielding an estimate of the explained proportion of variance attributable to each risk factor. Hypertension measures: Prior diagnosis of hypertension, systolic blood pressure, and diastolic blood pressure. Diabetes measures: Prior diagnosis of diabetes and glycated hemoglobin concentration. Obesity measures: body mass index and impedance-measured body fat percentage. Central adiposity measures: waist-hip ratio and impedance-measured trunk fat percentage. LDL: Low-density lipoprotein. HDL: High-density lipoprotein. Chronic kidney disease: glomerular filtration rate less than 60 mL/min/1.73m<sup>2</sup>. Female reproductive factors: history of menopause before age 40, preterm delivery, fetus with intrauterine growth retardation, gestational hypertension, pre-eclampsia, eclampsia, gestational diabetes, or polycystic ovary syndrome. Chronic inflammatory diseases: rheumatoid arthritis, psoriasis, lupus erythematosus, or human immunodeficiency virus infection. Socioeconomic measures: Average household income and Townsend Deprivation Index.

**Table IV:** Population attributable fractions of atherosclerotic cardiovascular disease risk

Risk Factor	Total			Men			Women		
	Population Attributable Fractions [95% CI]		P-het	Population Attributable Fractions [95% CI]		P-het	Population Attributable Fractions [95% CI]		P-het
	South Asians	Europeans		South Asians	Europeans		South Asians	Europeans	
Hypertension	0.40 [0.32 - 0.46]	0.34 [0.33 - 0.35]	0.113	0.35 [0.27 - 0.43]	0.30 [0.28 - 0.31]	0.183	0.45 [0.31 - 0.56]	0.33 [0.32 - 0.35]	0.076
Diabetes	0.22 [0.17 - 0.27]	0.07 [0.07 - 0.08]	<0.001	0.20 [0.14 - 0.25]	0.07 [0.06 - 0.07]	0.001	0.25 [0.15 - 0.34]	0.07 [0.06 - 0.08]	0.001
Chronic Kidney Disease	0.09 [0.06 - 0.12]	0.06 [0.06 - 0.07]	0.143	0.09 [0.05 - 0.12]	0.05 [0.05 - 0.06]	0.059	0.11 [0.03 - 0.18]	0.09 [0.08 - 0.1]	0.616
Chronic Inflammatory Diseases	0.01 [-0.01 - 0.02]	0.02 [0.01 - 0.02]	0.368	0.00 [-0.02 - 0.01]	0.01 [0.01 - 0.01]	0.098	0.06 [0.00 - 0.11]	0.03 [0.02 - 0.03]	0.261
Female Reproductive Factors	0.03 [-0.03 - 0.09]	0.05 [0.04 - 0.06]	0.645	-	-	-	0.03 [-0.03 - 0.09]	0.05 [0.04 - 0.06]	0.645
Obesity	0.04 [-0.01 - 0.08]	0.10 [0.09 - 0.11]	0.007	0.05 [0.00 - 0.10]	0.09 [0.08 - 0.10]	0.115	0.08 [-0.03 - 0.18]	0.11 [0.10 - 0.12]	0.576
Central Adiposity	0.50 [0.40 - 0.58]	0.39 [0.38 - 0.40]	0.018	0.36 [0.18 - 0.50]	0.33 [0.30 - 0.35]	0.684	0.37 [0.20 - 0.5]	0.21 [0.20 - 0.23]	0.048
High LDL Cholesterol	0.03 [-0.01 - 0.07]	0.07 [0.06 - 0.08]	0.135	0.04 [-0.01 - 0.08]	0.06 [0.05 - 0.07]	0.358	0.04 [-0.05 - 0.12]	0.11 [0.10 - 0.13]	0.077
Low HDL Cholesterol	0.10 [0.02 - 0.17]	0.09 [0.09 - 0.10]	0.889	0.09 [0.01 - 0.16]	0.08 [0.07 - 0.09]	0.895	0.24 [0.07 - 0.38]	0.13 [0.11 - 0.14]	0.155
High Triglycerides	0.16 [0.09 - 0.23]	0.17 [0.16 - 0.18]	0.813	0.06 [-0.03 - 0.15]	0.10 [0.09 - 0.12]	0.355	0.23 [0.10 - 0.35]	0.16 [0.14 - 0.17]	0.231

High C-reactive Protein	0.06 [0.00 - 0.11]	0.11 [0.10 - 0.12]	0.094	0.08 [0.02 - 0.13]	0.1 [0.09 - 0.11]	0.394	0.20 [0.05 - 0.32]	0.15 [0.14 - 0.17]	0.496
High Lipoprotein(a)	0.04 [0.00 - 0.07]	0.07 [0.06 - 0.07]	0.110	0.03 [-0.01 - 0.07]	0.07 [0.06 - 0.08]	0.129	0.08 [-0.01 - 0.16]	0.09 [0.07 - 0.10]	0.854
Family History	0.10 [0.02 - 0.16]	0.14 [0.13 - 0.15]	0.219	0.10 [0.02 - 0.17]	0.14 [0.13 - 0.16]	0.290	0.16 [0.00 - 0.30]	0.20 [0.18 - 0.22]	0.621
Current Smoking	0.04 [0.01 - 0.06]	0.07 [0.06 - 0.07]	0.042	0.01 [-0.03 - 0.05]	0.05 [0.04 - 0.06]	0.059	-0.01 [-0.03 - 0.02]	0.08 [0.07 - 0.09]	0.001
Unhealthy Diet	0.02 [-0.03 - 0.07]	0.10 [0.09 - 0.11]	0.002	-0.04 [-0.11 - 0.02]	0.05 [0.03 - 0.06]	0.007	0.05 [-0.05 - 0.14]	0.05 [0.03 - 0.06]	0.992
Sedentary Lifestyle	0.07 [0.02 - 0.11]	0.05 [0.05 - 0.06]	0.575	0.03 [-0.03 - 0.08]	0.03 [0.03 - 0.04]	0.773	0.09 [0.00 - 0.16]	0.02 [0.02 - 0.03]	0.135
Psychosocial Stressors	0.06 [-0.03 - 0.14]	0.02 [0.01 - 0.03]	0.357	0.09 [-0.01 - 0.18]	0.04 [0.02 - 0.05]	0.314	0.02 [-0.18 - 0.19]	0.03 [0.01 - 0.05]	0.946
Low Socioeconomic Status	0.22 [0.11 - 0.32]	0.28 [0.27 - 0.29]	0.259	0.19 [0.07 - 0.30]	0.25 [0.24 - 0.27]	0.321	0.38 [0.12 - 0.56]	0.43 [0.40 - 0.45]	0.657

Population attributable fractions for atherosclerotic cardiovascular disease risk factors stratified by ancestry and sex. LDL: Low-density lipoprotein. HDL: High-density lipoprotein. Chronic kidney disease: glomerular filtration rate less than 60 mL/min/1.73m<sup>2</sup>. Female reproductive factors: history of menopause before age 40, preterm delivery, fetus with intrauterine growth retardation, gestational hypertension, pre-eclampsia, eclampsia, gestational diabetes, or polycystic ovary syndrome. Chronic inflammatory diseases: rheumatoid arthritis, psoriasis, lupus erythematosus, or human immunodeficiency virus infection. P-heterogeneity (P-het) compares PAF estimates between ancestry groups and is deemed significant if <0.05.

**Table V:** Outpatient health care utilization and risk factor control in follow-up interval

	South Asians		Europeans		P-value
	Available n	Time-weighted Mean (SD)	Available n	Time-weighted Mean (SD)	
PCP Visits per year (mean, SD)	4,210	0.65 (0.9)	216,165	0.55 (1.3)	P < 0.001
LDL Cholesterol (mg/dL, mean (SD))	3,079	116.4 (31.7)	144,085	128.0 (32.9)	P < 0.001
Glycated Hemoglobin (% , mean (SD))	2,888	6.3 (1.1)	99,277	5.8 (0.8)	P < 0.001
Systolic Blood Pressure (mm Hg, mean (SD))	3,171	129.8 (11.9)	145,434	131.8 (12.6)	P < 0.001
Diastolic Blood Pressure (mm Hg, mean (SD))	3,220	78.4 (7.1)	159,277	78.2 (7.4)	P < 0.095

Summary of available outpatient data for healthcare utilization and time-weighted average risk factor measurements in follow-up period. PCP: Primary care physician. LDL: low-density lipoprotein. P-value is deemed significant if <0.05.

**Table VI:** Mediation analysis assessing association of risk factor variables with ancestry and incident atherosclerotic cardiovascular disease

Variable	Proportion mediated of ancestry association with ASCVD	P-Value
Hypertension	-0.005 [-0.015 - 0.004]	0.27
Systolic Blood Pressure	-0.036 [-0.060 - -0.023]	<0.001
Diastolic Blood Pressure	-0.022 [-0.039 - -0.013]	<0.001
Diabetes	0.001 [0.000 - 0.002]	0.16
Glycated Hemoglobin	0.095 [0.067 - 0.143]	<0.001
Glomerular Filtration Rate	0.100 [0.074 - 0.148]	<0.001
Chronic Inflammatory Diseases	-0.001 [-0.005 - 0.001]	0.28
Female Reproductive Factors	0.001 [-0.002 - 0.006]	0.35
Body Mass Index	0.023 [0.013 - 0.038]	0.97
Body Fat Percentage	0.001 [-0.040 - 0.043]	0.71
Waist-hip Ratio	0.008 [-0.013 - 0.032]	<0.001
Trunk Fat Percentage	-0.005 [-0.035 - 0.021]	0.49
LDL Cholesterol	-0.082 [-0.136 - -0.056]	<0.001
HDL Cholesterol	0.100 [0.072 - 0.150]	<0.001
Triglycerides	0.000 [-0.001 - 0.002]	0.64
Lipoprotein(a)	0.089 [0.065 - 0.136]	<0.001
C-reactive Protein	-0.002 [-0.007 - 0.004]	0.52
Family History of Heart Disease	0.015 [0.003 - 0.031]	0.01
Smoking	-0.086 [-0.142 - -0.062]	<0.001
Diet Score	-0.015 [-0.030 - -0.004]	0.01
Sedentary Time	0.002 [0.000 - 0.006]	0.07
Psychosocial Stressors	0.006 [0.001 - 0.012]	<0.001
Average Household Income	0.049 [0.032 - 0.082]	<0.001
Townsend Index	0.020 [0.011 - 0.035]	<0.001

Analyses testing the extent to which conventional cardiovascular risk factors mediate the associations of ancestry with atherosclerotic cardiovascular disease. For example, a proportion mediated of 0 would indicate that a risk factor does not mediate the ASCVD association with ancestry. P-value reflects whether the proportion of the association with ASCVD related to each risk factor is 0% (the null hypothesis) vs. not 0%. P-value is deemed significant if <0.05.